PCT REQUEST

Original (for SUBMISSION)

	· · · · · · · · · · · · · · · · · · ·	·
VIII-3-1	Declaration: Entitlement to claim priority Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application specified below, where the applicant is not the applicant who filed the earlier application or where the applicant's name has changed since the filing of the earlier application (Rules 4.17(iii) and 51bls.1(a)(iii))	in relation to this international application ONCOTHERAPY SCIENCE, INC.
		is entitled to claim priority of earlier application No. 60/538,658 by virtue of the following:
VIII-3-1		an assignment from NAKAMURA, Yusuke to
. v)		ONCOTHERAPY SCIENCE, INC., dated 20 January 2004 (20.01.2004)
VIII-3-1	1	an assignment from FURUKAWA, Yoichi to
,v)	`	ONCOTHERAPY SCIENCE, INC., dated 20
	<u> </u>	January 2004 (20.01.2004)
VIII-3-1 v)	Q 	an assignment from NAKAMURA, Yusuke to JAPAN AS REPRESENTED BY THE PRESIDENT OF THE UNIVERSITY OF TOKYO, dated 19 January 2004 (19.01.2004)
VIII-3-1	0	an assignment from FURUKAWA, Yoichi to
V)		JAPAN AS REPRESENTED BY THE PRESIDENT OF
		THE UNIVERSITY OF TOKYO, dated 19
		January 2004 (19.01.2004)
	ulari i la	THE PERSON OF SECTION
VIII-3-1 x)	(i This declaration is made for the purposes of:	AP: (BW GH GM KE LS MW MZ NA SD SL SZ 12 UG ZM ZW); EA: (AM AZ BY KG KZ MD RU TJ
^/	parposos on	TM); EP: (AT BE BG CH&LI CY CZ DE DK EE
		ES FI FR GB GR HU IE IT LU MC NL PL PT
		RO SE SI SK TR); OA: (BF BJ CF CG CI CM
		GA GN GQ GW ML MR NE SN TD TG); AE AG
		AL AM AT AU AZ BA BB BG BR BW BY BZ CA
		CHELI CN CO CR CU CZ DE DK DM DZ EC EE
		EG ES FI GB GD GE GH GM HR HU ID IL IN
		IS JP KE KG KP KR KZ LC LK LR LS LT LU
		LV MA MD MG MK MN MW MX MZ NA NI NO NZ
	<u>'</u>	OM PG PH PL PT RO RU SC SD SE SG SK SL
		SY TJ TM TN TR TT TZ UA UG UZ VC VN YU
	1	ZA ZM ZW

5/7

PCT REQUEST

Original (for SUBMISSION)

,	Declaration: Entitlement to claim priority Declaration as to the applicant's entitlement, as at the international filling date, to claim the priority of the earlier application specified below, where the applicant is not the applicant who filled the earlier application or where the applicant's name has changed since the filling of the earlier application (Rules 4.17(iii) and 51bis.1(a)(iii))	in relation to this international application
	Name	THE UNIVERSITY OF TOKYO
		is entitled to claim priority of earlier application No. 60/538,658 by virtue of the following:
VIII-3-2(vii)		transfer of entitlement from JAPAN AS REPRESENTED BY THE PRESIDENT OF THE UNIVERSITY OF TOKYO to THE UNIVERSITY OF TOKYO by way of Transfer of entitlement under the National University Corporation Law(Law No.112 of July 16, 2003), dated 01 April 2004 (01.04.2004)
	This declaration is made for the purposes of:	all designations

PATENT COOPERATION TREATY

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference ONC-A0310P	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2005/001172	International filing date (day/month/year) 21 January 2005 (21.01.2005)	Priority date (day/month/year) 23 January 2004 (23.01.2004)
International Patent Classification (8tl See relevant information in Form F	n edition unless older edition indicated) PCT/ISA/237	
Applicant ONCOTHERAPY SCIENCE, INC.		

1.	This international preliminary International Searching Author	report on patentability (Chapter I rity under Rule 44 <i>bis</i> .1(a).	l) is issued by the International Bureau on behalf of the
2.	This REPORT consists of a tot	al of 8 sheets, including this cov	er sheet.
	In the attached sheets, any refeto the international preliminary	rence to the written opinion of the report on patentability (Chapter	ne International Searching Authority should be read as a reference r I) instead.
3.	This report contains indication	s relating to the following items:	
	Box No. I	Basis of the report	
	Box No. II	Priority	
	Box No. III	Non-establishment of opini applicability	on with regard to novelty, inventive step and industrial
	Box No. IV	Lack of unity of invention	
	Box No. V	Reasoned statement under applicability; citations and	Article 35(2) with regard to novelty, inventive step or industrial explanations supporting such statement
	Box No. VI	Certain documents cited	
	Box No. VII	Certain defects in the intern	national application
	Box No. VIII	Certain observations on the	e international application
4.	The International Bureau will not, except where the applical date (Rule 44bis .2).	communicate this report to designt makes an express request under	gnated Offices in accordance with Rules 44his.3(c) and 93his.1 but er Article 23(2), before the expiration of 30 months from the priority
			Date of issuance of this report 24 July 2006 (24.07.2006)
	The International B		Authorized officer
1	34, chemin des (Masashi Honda

e-mail: pt08@wipo.int

Facsimile No. +41 22 338 82 70 Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

rom the NTERNATIONAL SEAF	OUNG AUTHO	RITY			REC'D 27	IUL 2005
				PC	WIPO	PCT
То:	•				· · · · · · · · · · · · · · · · · · ·	
see form f	PCT/ISA/220	1/8	INTERNATION	IAL SEAR PCT Rule 4	13 <i>bis</i> .1)	THORITY
Applicant's or agent's file			FOR FURTHER A	ACTION		
see form PCT/ISA/2		1 1 1 1 1 1			(day/month/year)	
International application PCT/JP2005/00117		International filing date (21.01.2005	ааулпонилуват)	23.01.200		
		both national classification	and IPC	1		
International Patent Class C12Q1/48, G01N33	ssification (IPC) or 8/574	DOBT REGULET CHEST MOSTOCION				
Applicant ONCOTHERAPY S	CIENCE, INC					
	entoine indical	tions relating to the fo	llowing items:			
1. This opinion of	ontains indicai	nons relating to the re				
→ M Box No. 1	Basis of the o	plnion				
	Priority		the results invent	ive eten and i	ndustrial applic	ability
☑ Box No. III		hment of opinion with re	gard to novelly, lilvely	uve step and i	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
☐ Box No. IV	Lack of unity	of invention	v 4/Vi) with rogard t	o povetty inv	entive step or it	ndustrial
⊠ Box No. V	Reasoned st applicability;	atement under Rule 43£ citations and explanatio	ons supporting such st	atement	2	
☐ Box No. VI	Certain docu					
☑ Box No. VI	Certain defe	cts in the international a	pplication		•	
☑ Box No. VI	II Certain obse	ervations on the internati	ional application			
2. FURTHER AC	CTION			,		
If a demand for written opinion the applicant of International E	n of the Internation chooses an Auth Bureau under Ru considered.	oreliminary examination in onal Preliminary Examination or the than this one one of the feet of the this one of the this one of the this one of the this of the th	e to be the IPEA and the opinions of this Inter	ne chosen IPE mational Sear	EA has notifed to ching Authority	the
If this opinion submit to the months from whichever ex	IPEA a written r the date of maili	above, considered to be eply together, where ap ng of Form PCT/ISA/220	e a written opinion of the propriate, with amend of or before the expirati	ne IPEA, the a ments, before ion of 22 mont	pplicant is invident the expiration ths from the pri	of three ority date,
For further or	otions, see Form	PCT/ISA/220.				
		to Form PCT/ISA/220.				•
			•			
Name and mailing a	dress of the ISA:		Authorized Office	r		Springs Pringing.
l					. •	. M.
6)) Europ	ean Patent Office 80 HV Rijswijk - P	- P.B. 5818 Patentlaan 2 Pays Bas	Jenkins, G			
Tel 4	21 70 340 - 2040 I	(X:3) coleponi	Telephone No. +	31 70 340-2608	;	eshaces sailo.
Fax: 4	31 70 340 - 3016	•				

_		
	Box	No. I Basis of the opinion
1.	With the la	regard to the language , this opinion has been established on the basis of the international application in anguage in which it was filed, unless otherwise indicated under this item.
	ì	This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2.	With nece	regard to any nucleotide and/or amino acid sequence disclosed in the international application and essary to the claimed invention, this opinion has been established on the basis of:
	a. typ	pe of material:
	×	a sequence listing
		atable(s) related to the sequence listing
	b. fo	rmat of material:
	2	in written format
	Œ	in computer readable form
	c. tın	ne of filing/furnishing:
	Ø	contained in the international application as filed.
	×	filed together with the international application in computer readable form.
		furnished subsequently to this Authority for the purposes of search.
3.		In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4	. Add	litional comments:
_	Вох	No. II Priority
1	. 🖾	The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2	. 🛮	This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3	. Add	litional observations, if necessary:

	No. III Non-establishment of licability	opir	nion with regard to novelty, inventive step and industrial
The obv	questions whether the claimed in ous), or to be industrially applica	nvent ble h	tion appears to be novel, to involve an inventive step (to be non ave not been examined in respect of:
	the entire international application	on,	
\boxtimes	claims Nos. 17-20		
bec	ause:		
	the said international application does not require an international	n, or t il pre	the said claims Nos. relate to the following subject matter which liminary examination (specify):
	the description, claims or drawing unclear that no meaningful opin	ngs (i ion c	indicate particular elements below) or said claims Nos. are so ould be formed (specify):
	the claims, or said claims Nos. could be formed.	are s	o inadequately supported by the description that no meaningful opinion
\boxtimes	no international search report h	as be	een established for the whole application or for said claims Nos. 17-20
	the nucleotide and/or amino aci C of the Administrative Instructi	d sec	quence listing does not comply with the standard provided for in Annex in that:
,	the written form		has not been furnished
			does not comply with the standard
	the computer readable form		has not been furnished
			does not comply with the standard
	the tables related to the nucleo not comply with the technical re	itide a equir	and/or amino acid sequence listing, if in computer readable form only, do ements provided for in Annex C-bis of the Administrative Instructions.
	See separate sheet for further	detai	ils

Box No. V Reasoned statement under Rule 43bis.1(a)(l) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

5,7,9-11,13-15

No:

Claims

1-4,6,8,12,16

Inventive step (IS)

Yes: Claims

No: Claims

1-16

Industrial applicability (IA)

Yes: Claims

1-16

No: Claims

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 DOCUMENTS

- D1: WO 02/090578 A (CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED; CHROMA THERAPEUTICS L) 14 November 2002 (2002-11-14)
- D2: REA STEPHEN ET AL: "Regulation of chromatin structure by site-specific histone H3 methyltransferases" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 406, no. 6796, August 2000 (2000-08), pages 593-599, XP002154907 ISSN: 0028-0836

2 NOVELTY

- The polypeptide alluded to in claims 1-14 is neither structurally limited (e.g. claim 1.a.ii clearly covers any polypeptide sequence), nor functionally limited (all proteins share certain biological activities such as nutritional value). In sum, the polypeptide of claims 1-14 could be anything. As a result, the subject-matter of claims 1-4,6,8,12 is not novel in the sense of Article 33(2) PCT. D1 discloses: a method of measuring methyl transferase activity of SET proteins such as SET1 and SET2 using H3 lys 4 as a substrate and S-adenosyl-L-methionine as a cofactor (p. 51,52). A corresponding method, and implicitly a kit, for screening for modulators of methyl transferase activity is also disclosed (claims 2,3), as well as the use of the modulators in the treatment of cancers such as colon cancer (p. 34). Therefore, the subject-matter of claims 1-4,6,8,12 is not new in the sense of Article 33(2) PCT.
- Furthermore, D1 discloses a peptide containing NHSCDPN (figure 1, sequence 6, NHSC region) and S-adenosyl-L-methionine (p. 51). Therefore, the subject-matter of claim 16 is not new in the sense of Article 33(2) PCT.
- 5 INVENTIVE STEP
- Although the discovery that ZNFN3A1 has methyl transferase activity would appear not to be obvious from the prior art (D1, p. 2, paragraph 3; D2, p. 595, column 2,

paragraph 1, last sentence), the broad definition of the polypeptide renders the subject-matter of claims 5,7,9-11,13-15 either obvious in light of D1, or unlikely to be a solution to any technical problem over the whole of the claimed scope (see Item VIII). Consequently, the subject-matter of said claims is not inventive (Article 33(3) PCT).

- 7 INDUSTRIAL APPLICABILITY
- The subject-matter of claims 1-16 is considered industrially applicable in the field of medicine (Article 33(4) PCT).

Re Item VII

Certain defects in the international application

9 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

Re Item VIII

Certain observations on the international application

The scope of the claims must be commensurate with the contribution to the prior art (PCT Guidelines 5.52). In this case, the application shows that ZNFN3A1 (surprisingly) has methyl transferase activity. However, the subject-matter of claims 1-14 extends to methods and kits involving any polypeptide. The methods and kits of claims 1-12 can plainly only work if the biological activity is methyl transferase activity, and the methods and kits of claims 13,14 can only work if the biological activity is affinity for HSP90A - i.e. the biological activity cannot simply be any biological activity. Furthermore, based upon the disclosure of the application, the skilled person would only reasonably consider using sequence variants that are closely related to wild-type ZNFN3A1 to find polypeptides with the aforementioned functions, at least more closely related to ZNFN3A1 than to a protein derived from a completely different gene - not any sequence variant as implied by expressions such as in claim 1.a.ii (any number of mutations). As such, the subject-matter of claims 1-14 is unsupported (Article 6 PCT), and undisclosed (Article 5 PCT) within

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/JP2005/001172

the application as a whole.

- 11 The approximate term "about" (at least about 80% homology) used in claims 1,8,9,13-15 is contrary to the requirements of clarity of Article 6 PCT.
- The claims contain many expressions that are linguistically unclear (Article 6 PCT). As just a few cases in point: "the condition capable of methylation of the substrate" (claim 1,5,8), "an at least methylation region" (claim 2,10).
- 13 The subject-matter of claim 12 is dependent on claim 7. However, it would appear that it should be dependent on claim 8 instead. This results in a lack of clarity according to Article 6 PCT.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

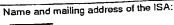
Applicant's or agent's file reference ONC-A0310P	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2005/001172	International filing date (day/month/year) 21 January 2005 (21.01.2005)	Priority date (day/month/year) 23 January 2004 (23.01.2004)
International Patent Classification (8t See relevant information in Form I	h edition unless older edition indicated) PCT/ISA/237	
Applicant ONCOTHERAPY SCIENCE, INC.		

1.	This international preliminary rep International Searching Authority	ort on patentability (Chapter I) under Rule 44 bis.1(a).	is issued by the International Bureau on behalf of the
2.	This REPORT consists of a total in the attached sheets, any referent to the international preliminary re-	nce to the written opinion of the	e International Searching Authority should he read as a reference
3.	This report contains indications r	elating to the following items:	
	Box No. I	Basis of the report	
	Box No. II	Priority	
	Box No. III	Non-establishment of opinic applicability	on with regard to novelty, inventive step and industrial
	Box No. IV	Lack of unity of invention	
	Box No. V	Reasoned statement under A applicability; citations and o	Article 35(2) with regard to novelty, inventive step or industrial explanations supporting such statement
	Box No. VI	Certain documents cited	
	Box No. VII	Certain defects in the intern	ational application
	Box No. VIII	Certain observations on the	international application
4.	The International Bureau will conot, except where the applicant date (Rule 44bis .2).	ommunicate this report to designates an express request unde	gnated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but r Article 23(2), before the expiration of 30 months from the priority
<u> </u>			
		ļ	Date of issuance of this report 24 July 2006 (24.07.2006)
	The International Bur	eau of WIPO	Authorized officer
	34, chemin des Co 1211 Geneva 20, S	lombettes	Masashi Honda
Face	simile No. +41 22 338 82 70		e-mail: pt08@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

REC'D 27 JUL 2005 From the INTERNATIONAL SEARCHING AUTHORITY WIPO To: WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY see form PCT/ISA/220 (PCT Rule 43bis.1) Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet) FOR FURTHER ACTION Applicant's or agent's file reference See paragraph 2 below see form PCT/ISA/220 Priority date (day/month/year) International filing date (day/month/year) International application No. 23.01.2004 21.01.2005 PCT/JP2005/001172 International Patent Classification (IPC) or both national classification and IPC C12Q1/48, G01N33/574 Applicant ONCOTHERAPY SCIENCE, INC. This opinion contains indications relating to the following items: Basis of the opinion Box No.
 I ☑ Box No. II Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☑ Box No. III Lack of unity of invention Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial ☐ Box No. IV applicability; citations and explanations supporting such statement Box No. V Certain documents cited Box No. VI Certain defects in the international application Box No. VII Box No. VIII Certain observations on the international application **FURTHER ACTION** If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. For further details, see notes to Form PCT/ISA/220.



Authorized Officer

<u>a</u>

European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016

Jenkins, G

Telephone No. +31 70 340-2608



_	Box N	o. I Basis of the opinion
1.	With re	egard to the language , this opinion has been established on the basis of the international application in guage in which it was filed, unless otherwise indicated under this item.
	la	nis opinion has been established on the basis of a translation from the original language into the following nguage , which is the language of a translation furnished for the purposes of international search nder Rules 12.3 and 23.1(b)).
2.	With r	egard to any nucleotide and/or amino acid sequence disclosed in the international application and sary to the claimed invention, this opinion has been established on the basis of:
	a. type	e of material:
	\boxtimes	a sequence listing
		table(s) related to the sequence listing
	b. for	nat of material:
	3	in written format
•	. 🖸	in computer readable form
	c. tım	e of filing/furnishing:
	⋈	contained in the international application as filed.
	Ø	filed together with the international application in computer readable form.
		furnished subsequently to this Authority for the purposes of search.
3	į	n addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4	I. Addi	tional comments:
-	Вох	No. II Priority
-		The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
	2. 🏻	This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43 <i>bis</i> .1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
	3. Add	itional observations, if necessary:

	No. III Non-establishment of	opin	nion with regard to novelty, inventive step and industrial
app	licability		
The obv	questions whether the claimed in ous), or to be industrially applica	nvent ble h	ion appears to be novel, to involve an inventive step (to be non ave not been examined in respect of:
	the entire international application,		
\boxtimes	claims Nos. 17-20		
bec	ause:		
	the said international application does not require an international	n, or t Il prel	the said claims Nos. relate to the following subject matter which iminary examination (specify):
	the description, claims or drawing unclear that no meaningful opin	ngs <i>(i</i> ion c	indicate particular elements below) or said claims Nos. are so ould be formed (specify):
	the claims, or said claims Nos. could be formed.	are s	o inadequately supported by the description that no meaningful opinion
\boxtimes	no international search report h	as be	een established for the whole application or for said claims Nos. 17-20
	the nucleotide and/or amino aci C of the Administrative Instructi	d sec	quence listing does not comply with the standard provided for in Annex n that:
	the written form		has not been furnished
			does not comply with the standard
	the computer readable form		has not been furnished
	·		does not comply with the standard
	the tables related to the nucleon not comply with the technical re	otide a equir	and/or amino acid sequence listing, if in computer readable form only, do ements provided for in Annex C- <i>bis</i> of the Administrative Instructions.
	See separate sheet for further	detai	ils

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

5,7,9-11,13-15

No:

Claims

1-4,6,8,12,16

Inventive step (IS)

Yes: Claims

Claims

1-16

Industrial applicability (IA)

Yes: Claims

No:

1-16

No: Claims

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 DOCUMENTS

- D1: WO 02/090578 A (CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED; CHROMA THERAPEUTICS L) 14 November 2002 (2002-11-14)
- D2: REA STEPHEN ET AL: "Regulation of chromatin structure by site-specific histone H3 methyltransferases" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 406, no. 6796, August 2000 (2000-08), pages 593-599, XP002154907 ISSN: 0028-0836

2 NOVELTY

- The polypeptide alluded to in claims 1-14 is neither structurally limited (e.g. claim 1.a.ii clearly covers any polypeptide sequence), nor functionally limited (all proteins share certain biological activities such as nutritional value). In sum, the polypeptide of claims 1-14 could be anything. As a result, the subject-matter of claims 1-4,6,8,12 is not novel in the sense of Article 33(2) PCT. D1 discloses: a method of measuring methyl transferase activity of SET proteins such as SET1 and SET2 using H3 lys 4 as a substrate and S-adenosyl-L-methionine as a cofactor (p. 51,52). A corresponding method, and implicitly a kit, for screening for modulators of methyl transferase activity is also disclosed (claims 2,3), as well as the use of the modulators in the treatment of cancers such as colon cancer (p. 34). Therefore, the subject-matter of claims 1-4,6,8,12 is not new in the sense of Article 33(2) PCT.
- Furthermore, D1 discloses a peptide containing NHSCDPN (figure 1, sequence 6, NHSC region) and S-adenosyl-L-methionine (p. 51). Therefore, the subject-matter of claim 16 is not new in the sense of Article 33(2) PCT.
- 5 INVENTIVE STEP
- Although the discovery that ZNFN3A1 has methyl transferase activity would appear not to be obvious from the prior art (D1, p. 2, paragraph 3; D2, p. 595, column 2,

paragraph 1, last sentence), the broad definition of the polypeptide renders the subject-matter of claims 5,7,9-11,13-15 either obvious in light of D1, or unlikely to be a solution to any technical problem over the whole of the claimed scope (see Item VIII). Consequently, the subject-matter of said claims is not inventive (Article 33(3) PCT).

- 7 INDUSTRIAL APPLICABILITY
- The subject-matter of claims 1-16 is considered industrially applicable in the field of medicine (Article 33(4) PCT).

Re Item VII

Certain defects in the international application

9 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

Re Item VIII

Certain observations on the international application

The scope of the claims must be commensurate with the contribution to the prior art (PCT Guidelines 5.52). In this case, the application shows that ZNFN3A1 (surprisingly) has methyl transferase activity. However, the subject-matter of claims 1-14 extends to methods and kits involving any polypeptide. The methods and kits of claims 1-12 can plainly only work if the biological activity is methyl transferase activity, and the methods and kits of claims 13,14 can only work if the biological activity is affinity for HSP90A - i.e. the biological activity cannot simply be any biological activity. Furthermore, based upon the disclosure of the application, the skilled person would only reasonably consider using sequence variants that are closely related to wild-type ZNFN3A1 to find polypeptides with the aforementioned functions, at least more closely related to ZNFN3A1 than to a protein derived from a completely different gene - not any sequence variant as implied by expressions such as in claim 1.a.ii (any number of mutations). As such, the subject-matter of claims 1-14 is unsupported (Article 6 PCT), and undisclosed (Article 5 PCT) within

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/JP2005/001172

the application as a whole.

- The approximate term "about" (at least about 80% homology) used in claims 1,8,9,13-15 is contrary to the requirements of clarity of Article 6 PCT.
- The claims contain many expressions that are linguistically unclear (Article 6 PCT). As just a few cases in point: "the condition capable of methylation of the substrate" (claim 1,5,8), "an at least methylation region" (claim 2,10).
- 13 The subject-matter of claim 12 is dependent on claim 7. However, it would appear that it should be dependent on claim 8 instead. This results in a lack of clarity according to Article 6 PCT.

PATENT COOPERATION TREATY

rom the VTERNATIONAL SEARCHING AUTHORITY	,	REC'D 2 7 JUL 2005
To:		PC WIPO PCT
see form PCT/ISA/220	INTERNATIO	ITTEN OPINION OF THE ONAL SEARCHING AUTHORITY (PCT Rule 43 bis.1) see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220	FOR FURTHE See paragraph 2	below
	ernational filing date (day/month/year) .01.2005	Priority date (day/month/year) 23.01.2004
International Patent Classification (IPC) or both C12Q1/48, G01N33/574	national classification and IPC	
Applicant ONCOTHERAPY SCIENCE, INC.		
□ Box No. IV Lack of unity of in □ Box No. V Reasoned statem applicability; citati □ Box No. VI Certain documen □ Box No. VII Certain defects in □ Box No. VIII Certain observati 2. FURTHER ACTION If a demand for international prelim written opinion of the International the applicant chooses an Authority International Bureau under Rule 6 will not be so considered.	on the opinion with regard to novelty, invention tent under Rule 43bis.1(a)(i) with regard to novelty, invention tent under Rule 43bis.1(a)(i) with regard to said explanations supporting such that international application ons on the international application ons on the international application preliminary examination is made, this opinion of the IPEA are 3.1bis(b) that written opinions of this like, considered to be a written opinion of together, where appropriate, with a metal form PCT/ISA/220 or before the explanation.	on will usually be considered to be a EA"). However, this does not apply where

Name and mailing address of the ISA:

Authorized Officer

<u></u>

European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016

Jenkins, G

Telephone No. +31 70 340-2608



_							
	Box	No. I	Basis of the opinion				
٦.	. With regard to the language , this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.						
	l	langua	pinion has been established on the basis of a translation from the original language into the following age , which is the language of a translation furnished for the purposes of international search r Rules 12.3 and 23.1(b)).				
2.	With nece	regar essary	d to any nucleotide and/or amino acid sequence disclosed in the international application and to the claimed invention, this opinion has been established on the basis of:				
	a. type of material:						
	×	as	sequence listing				
] tat	ble(s) related to the sequence listing				
	b. fo	rmat o	of material:				
	· 🖸	in in	written format				
	. ©] in	computer readable form				
	c. time of filling/furnishing:						
	6	₫ co	ntained in the international application as filed.				
	[2	3 file	ed together with the international application in computer readable form.				
	Œ] fu	rnished subsequently to this Authority for the purposes of search.				
3.	. 0	has b	dition, in the case that more than one version or copy of a sequence listing and/or table relating thereto been filed or furnished, the required statements that the information in the subsequent or additional is is identical to that in the application as filed or does not go beyond the application as filed, as oppriate, were furnished.				
4. Additional comments:							
_	Box	No.	ll Priority				
1	. 🖾	does	validity of the priority claim has not been considered because the International Searching Authority not have in its possession a copy of the earlier application whose priority has been claimed or, where ired, a translation of that earlier application. This opinion has nevertheless been established on the mption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.				
2	. 🗆	has b	opinion has been established as if no priority had been claimed due to the fact that the priority claim been found invalid (Rules 43 bis.1 and 64.1). Thus for the purposes of this opinion, the international date indicated above is considered to be the relevant date.				
3	. Add	ditiona	d observations, if necessary:				

	No. III Non-establishment of cability	opin	ion with regard to novelty, inventive step and industrial			
The o	questions whether the claimed in ous), or to be industrially applical	nvent ble ha	ion appears to be novel, to involve an inventive step (to be non ave not been examined in respect of:			
	the entire international application,					
⊠ (claims Nos. 17-20					
beca	use:					
	the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):					
	the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):					
	the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.					
\boxtimes	no international search report h	as be	een established for the whole application or for said claims Nos. 17-20			
	the nucleotide and/or amino aci	nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Aif the Administrative Instructions in that:				
	the written form		has not been furnished			
			does not comply with the standard			
	the computer readable form		has not been furnished			
	•		does not comply with the standard			
	the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form of comply with the technical requirements provided for in Annex C-bis of the Administrative Instruction					
	See separate sheet for further	deta	ils			

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

5,7,9-11,13-15

No: Claims

1-4,6,8,12,16

Inventive step (IS)

Yes: Claims

No: Claims

1-16

Industrial applicability (IA)

Yes: Claims

1-16

No: Claims

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 DOCUMENTS

- D1: WO 02/090578 A (CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED: CHROMA THERAPEUTICS L) 14 November 2002 (2002-11-14)
- D2: REA STEPHEN ET AL: "Regulation of chromatin structure by site-specific histone H3 methyltransferases" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 406, no. 6796, August 2000 (2000-08), pages 593-599, XP002154907 ISSN: 0028-0836

2 NOVELTY

- The polypeptide alluded to in claims 1-14 is neither structurally limited (e.g. claim 1.a.ii clearly covers any polypeptide sequence), nor functionally limited (all proteins share certain biological activities such as nutritional value). In sum, the polypeptide of claims 1-14 could be anything. As a result, the subject-matter of claims 1-4,6,8,12 is not novel in the sense of Article 33(2) PCT. D1 discloses: a method of measuring methyl transferase activity of SET proteins such as SET1 and SET2 using H3 lys 4 as a substrate and S-adenosyl-L-methionine as a cofactor (p. 51,52). A corresponding method, and implicitly a kit, for screening for modulators of methyl transferase activity is also disclosed (claims 2,3), as well as the use of the modulators in the treatment of cancers such as colon cancer (p. 34). Therefore, the subject-matter of claims 1-4,6,8,12 is not new in the sense of Article 33(2) PCT.
- Furthermore, D1 discloses a peptide containing NHSCDPN (figure 1, sequence 6, NHSC region) and S-adenosyl-L-methionine (p. 51). Therefore, the subject-matter of claim 16 is not new in the sense of Article 33(2) PCT.
- 5 INVENTIVE STEP
- Although the discovery that ZNFN3A1 has methyl transferase activity would appear not to be obvious from the prior art (D1, p. 2, paragraph 3; D2, p. 595, column 2,

paragraph 1, last sentence), the broad definition of the polypeptide renders the subject-matter of claims 5,7,9-11,13-15 either obvious in light of D1, or unlikely to be a solution to any technical problem over the whole of the claimed scope (see Item VIII). Consequently, the subject-matter of said claims is not inventive (Article 33(3) PCT).

- 7 INDUSTRIAL APPLICABILITY
- The subject-matter of claims 1-16 is considered industrially applicable in the field of medicine (Article 33(4) PCT).

Re Item VII

Certain defects in the international application

9 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

Re Item VIII

Certain observations on the international application

The scope of the claims must be commensurate with the contribution to the prior art (PCT Guidelines 5.52). In this case, the application shows that ZNFN3A1 (surprisingly) has methyl transferase activity. However, the subject-matter of claims 1-14 extends to methods and kits involving any polypeptide. The methods and kits of claims 1-12 can plainly only work if the biological activity is methyl transferase activity, and the methods and kits of claims 13,14 can only work if the biological activity is affinity for HSP90A - i.e. the biological activity cannot simply be any biological activity. Furthermore, based upon the disclosure of the application, the skilled person would only reasonably consider using sequence variants that are closely related to wild-type ZNFN3A1 to find polypeptides with the aforementioned functions, at least more closely related to ZNFN3A1 than to a protein derived from a completely different gene - not any sequence variant as implied by expressions such as in claim 1.a.ii (any number of mutations). As such, the subject-matter of claims 1-14 is unsupported (Article 6 PCT), and undisclosed (Article 5 PCT) within

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From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Тα

SHIMIZU, Hatsushi Kantetsu Tsukuba Bldg. 6F 1-1-1, Oroshi-machi Tsuchiura-shi, Ibaraki 3000847

Date of mailing (day/month/year) 12 April 2005 (12.04.2005)		
Applicant's or agent's file reference ONC-A0310P	IMPORTANT NOTIFICATION	
International application No. PCT/JP05/001172	International filing date (day/month/year) 21 January 2005 (21.01.2005)	
International publication date (day/month/year)	Priority date (day/month/year) 23 January 2004 (23.01.2004)	
Applicant ONCOTH	IERAPY SCIENCE, INC. et al	

- 1. By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- 2. (If applicable) The letters "NR" appearing in the right-hand column denote a priority document which, on the date of mailing of this. Form, had not yet been received by the International Bureau under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- 3. (If applicable) An asterisk (*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b) (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as the priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date Priority application No. Country or regional Office or PCT receiving Office of priority document

23 January 2004 (23.01.2004) 60/538,658 US 03 March 2005 (03.03.2005)

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Form PCT/1B/304 (January 2004)